



PATENT

Attorney Docket No.: A-63708-6/TAL/NHT

Attorney File No.: 465840-00524

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

BUELOW et al.

Serial No. 10/782,260

Filing Date: February 18, 2004

For: *Methods For Enhancing Graft
Survival by Modulating Heme
Oxygenase Activity*

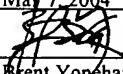
Examiner: Not Yet Assigned

Art Unit: 1632

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Dated: May 7, 2004

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INFORMATION DISCLOSURE STATEMENT

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

In satisfaction of the duty of disclosure under 37 C.F.R. § 1.56, and in accordance with the provisions of 37 C.F.R. §§ 1.97 and 1.98, Applicants wish to draw the attention of the U.S. Patent and Trademark Office to the references cited on the accompanying form PTO/SB/8A. In accordance with 1273 Off. Gaz. Pat. Off. 1, 8/5/2003, no copies of U.S. patents and U.S. published applications are enclosed. Copies of all other references are enclosed.

Further, this application is a continuation of the following related U.S. Application – Serial No. 09/515,582, filed February 29, 2000 (pending). Applicant wishes to draw the attention of the U.S. Patent and Trademark Office to the references cited on the accompanying substitute for form PTO-1449 marked with an asterisk (*). Since these references were previously disclosed in the above-mentioned application, in accordance with 37 C.F.R. § 1.98(d), no copies of these references are enclosed.

Serial No. 10/782,260
Filing Date: February 18, 2004

None of the foregoing references are believed to disclose the invention as claimed.

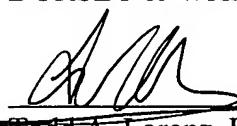
Nothing herein shall constitute an admission concerning the contents of any of the cited references, nor shall the inclusion of a reference herein be considered an admission that the reference constitutes prior art against the invention claimed in the above-identified application. Submission of the present document shall not be construed as an admission that a search has been made or that better art does not exist.

As far as is known to the undersigned, this Information Disclosure Statement is being filed within three months of the filing date of a national application, within three months of the date of entry of the national state in an international application, or before the mailing date of a first Office Action on the merits as set forth in 37 C.F.R. § 1.97(b), and therefore no fee is required. While no fee is believed to be due, if this belief is in error the Commissioner is authorized to charge any additional fees, including extension fees or other relief which may be required, or credit any overpayment to Deposit Account No. 50-2319 (Our Order No. 465840-00524 [A-63708-6/TAL/NHT]).

Respectfully submitted,

DORSEY & WHITNEY LLP

BY:


Todd A. Lorenz, Reg. No. 39,754

Dated: 5/6/04

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Attachments : Form PTO/SB/8A, Substitute for form 1449
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STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet

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Complete if KnownSubstitute for form 1449A/PTO
(Modified)

| | |
|----------------------|-------------------|
| Application Number | 10/782,260 |
| Filing Date | February 18, 2004 |
| First Named Inventor | BUELOW, Roland |
| Art Unit | To be assigned |
| Examiner Name | To be assigned |

Attorney Docket Number 33861/US/TAL/NHT ([A-63708-6] 465840-524)

U.S. PATENT DOCUMENTS

| Examiner Initials* | Cite No. ¹ | Document Number Number-Kind Code ² (if known) | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
|--------------------|-----------------------|---|--------------------------------|---|---|
| A1 * | | 4,829,984 | 05-16-1989 | Gordon | |
| A2 * | | 5,563,132 | 10-08-1996 | Bodenass | |
| A3 * | | 5,756,492 | 05-26-1998 | Buelow et al. | |
| A4 * | | 6,013,641 | 01-11-2000 | Lussow et al. | |
| A5 * | | 6,060,467 | 05-09-2000 | Buelow | |

FOREIGN PATENT DOCUMENTS

| Examiner Initials* | Cite No. ¹ | Foreign Patent Document Country Code ⁴ Number ⁴ Kind Code ⁵ (if known) | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | T ⁶ |
|--------------------|-----------------------|---|--------------------------------|---|---|----------------|
| B1 * | | WO 96/09038 A2 | 03-28-1996 | William Harvey Research Ltd. | | |
| B2 | | WO 98/09618 A2/A3 | 03-12-1998 | SangStat Medical Corporation | | |
| B3 | | WO 99/23215 A2/A3 | 05-14-1999 | University of Florida | | |
| B4 | | WO 00/12118 A2/A3 | 03-09-2000 | President & Fellows of Harvard College | | |

NON PATENT LITERATURE DOCUMENTS

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|--------------------|-----------------------|---|----------------|
| C1 | | ABRAHAM, N.G., et al., "Retinal pigment epithelial cell-based gene therapy against hemoglobin toxicity," <i>Int. J. Mol. Med.</i> 1:657-663 (1998). | |
| C2 | | ABRAHAM, N.G., et al., "The physiological significance of heme oxygenase," <i>Int. J. Biochem.</i> 20(6):543-558 (1988). | |
| C3 | | AGARWAL, A., et al., "Gas-generating systems in acute renal allograft rejection in the rat," <i>Transplantation</i> 61(1):93-98 (Jan. 1996). | |
| C4 * | | ALBERTS, B., et al., "Chapter 3: Macromolecules: Structure, Shape, and Information," <i>Molecular Biology of the Cell</i> , B. Alberts et al. (eds.), 3 rd ed., pp. 122-123, Garland Publishing, Inc.: New York, NY (1994). | |
| C5 | | AMERSI, F., et al., "Carbon monoxide provides protection against ischemia/reperfusion injury in rat livers," No. 156, <i>Conf. Proc. Transplant 2001</i> , The Joint American Transplant Meeting, Chicago, IL (May 11 - 16, 2001). | |
| C6 * | | AMERSI, F., et al., "Upregulation of heme oxygenase-1 protects genetically fat Zukcer rat livers from ischemia/reperfusion injury," <i>J. Clin. Invest.</i> 104(11):1631-1639 (Dec. 1999). | |
| C7 * | | ARHEHALI, A., et al., "Direct gene transfer into donor hearts at the time of harvests," <i>J. Thorac. Cardiovasc. Surg.</i> 109(4):716-719 (1995). | |
| C8 * | | BENTZ, J., et al., "DINAMO: interactive protein alignment and model building," <i>Bioinformatics</i> 15(4):309-316 (1999). | |
| C9 * | | BLYDT-HANSEN, T.D., et al., "Heme oxygenase-1 gene transfer protects against ischemia/reperfusion injury in rat renal isograft model," No. 157, <i>Conf. Proc. Transplant 2001</i> , The Joint American Transplant Meeting, Chicago, IL (May 11 - 16, 2001). | |

| Examiner Signature | Date Considered |
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| <p style="text-align: center;">Substitute for form 1449A/PTO (Modified)</p> <p style="text-align: center;">INFORMATION DISCLOSURE STATEMENT BY APPLICANT</p> <p style="text-align: center;">(use as many sheets as necessary)</p> | | | | <p style="text-align: center;">Complete if Known</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%;">Application Number</td> <td style="width: 50%;">10/782,260</td> </tr> <tr> <td>Filing Date</td> <td>February 18, 2004</td> </tr> <tr> <td>First Named Inventor</td> <td>BUELOW, Roland</td> </tr> <tr> <td>Art Unit</td> <td>To be assigned</td> </tr> <tr> <td>Examiner Name</td> <td>To be assigned</td> </tr> </table> | | Application Number | 10/782,260 | Filing Date | February 18, 2004 | First Named Inventor | BUELOW, Roland | Art Unit | To be assigned | Examiner Name | To be assigned |
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| Sheet | 2 | of | 6 | Attorney Docket Number | | | | | | | | | | | |
| 33861/US/TAL/NHT ([A-63708-6] 465840-524) | | | | | | | | | | | | | | | |

| NON PATENT LITERATURE DOCUMENTS | | |
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| Examiner Initials* | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. |
| | C10 * | BOASQUEVISQUE, C., et al., "Ex vivo liposome-mediated gene transfer to lung isografts," <i>J. Thorac. Cardiovasc. Surg.</i> 115(1):38-44 (Jan. 1998). |
| | C11 * | BOUCHER, R., "Status of gene therapy for cystic fibrosis lung disease," <i>J. Clin. Invest.</i> 103(4):441-445 (Feb. 1999). |
| | C12 * | BOWIE, J., et al., "Deciphering the Message in Protein Sequences: Tolerance to Amino Acid Substitutions," <i>Science</i> 247:1306-1310 (Mar. 1990). |
| | C13 * | BRAUNER, R., et al., "Intracoronary adenovirus-mediated transfer of immunosuppressive cytokine genes prolongs allograft survival," <i>J. Thorac. Cardiovasc. Surg.</i> 114(6):923-933 (Dec. 1997). |
| | C14 | BROUARD, S., et al., "Carbon monoxide generated by heme oxygenase-1 suppresses endothelial cell apoptosis through a P38 mark dependent mechanism," No. 1027, <i>Conf. Proc. Transplant 2001</i> , The Joint American Transplant Meeting, Chicago, IL (May 11 - 16, 2001). |
| | C15 * | BÜELER, H., "Adeno-associated viral vectors for gene transfer and gene therapy," <i>Biol. Chem.</i> 380(6):613-622 (1999). |
| | C16 * | CHAVEAU, C., et al., "Heme oxygenase-1 (HO-1) gene transfer delayed allograft acute rejection in a rat model," No. 36, <i>Conf. Proc. Transplant 2001</i> , The Joint American Transplant Meeting, Chicago, IL (May 11 - 16, 2001). |
| | C17 | COITO, A., et al., "Heme oxygenase-1 gene transfer inhibits inducible nitric oxide synthase expression and protects genetically fat Zucker rat livers from ischemia/reperfusion injury," No. 155, <i>Conf. Proc. Transplant 2001</i> , The Joint American Transplant Meeting, Chicago, IL (May 11 - 16, 2001). |
| | C18 * | CRYSTAL, R.G., "Transfer of genes to humans: early lessons and obstacles to success," <i>Science</i> 270(5235):404-410 (Oct. 1995). |
| | C19 | CUTURI, M., et al., "RDP1258, a New Rationally Designed Immunosuppressive Peptide, Prolongs Allograft Survival in Rats: Analysis of Its Mechanism of Action," <i>Mol. Med.</i> 5(12):820-832 (Dec. 1999). |
| | C20 | DEAN, P., et al., "Induction of heme oxygenase-1 with cobalt protoporphyrin fails to prolong hamster-to-rat kidney xenograft survival," No. 1266, <i>Conf. Proc. Transplant 2001</i> , The Joint American Transplant Meeting, Chicago, IL (May 11 - 16, 2001). |
| | C21 * | DeBRUYNE, L., et al., "Gene transfer of immunomodulatory peptides correlates with heme oxygenase-1 induction and enhanced allograft survival," <i>Transplantation</i> 69(1):120-128 (Jan. 2000). |
| | C22 | DeBRUYNE, L., et al., "Lipid-mediated gene transfer of viral IL-10 prolongs vascularized cardiac allograft survival by inhibiting donor-specific cellular and humoral immune response," <i>Gene Ther.</i> 5(8):1079-1087 (Aug. 1998). |
| | C23 | DRUMMOND, G., et al., "Prevention of neonatal hyperbilirubinemia by tin protoporphyrin IX, a potent competitive inhibitor of heme oxidation," <i>Proc. Natl. Acad. Sci. USA</i> 78(10):6466-6470 (Oct. 1981). |
| | C24 * | ECK, et al., "Chapter 5," <i>Goodman and Gilman's The Pharmacological Basis of Therapeutics</i> , 9 th ed., pp. 77-101, McGraw Hill: New York, NY (1995). |
| | C25 * | EVANS, C-O, et al., "Cloning and sequencing and expression of cDNA for chick liver heme oxygenase: comparison of avian and mammalian cDNAs and deduced protein," <i>Biochem. J.</i> 273:659-666 (1991). |
| | C26 * | HAGA, Y., et al., "Unconjugated bilirubin inhibits <i>in vitro</i> major histocompatibility complex-unrestricted cytotoxicity of human lymphocytes," <i>Biochim. Biophys. Acta</i> 1316:29-34 (1996). |
| | C27 | HANCOCK, W., et al., "Antibody-induced transplant arteriosclerosis is prevented by graft expression of anti-oxidant and anti-apoptotic genes," <i>Nat. Med.</i> 4(12):1392-1396 (Dec. 1998). |
| | C28 * | HEGAZY, K.A., et al., "Functional human heme oxygenase has a neuroprotective effect on adult rat ganglion cells after pressure induced ischemia," <i>NeuroReport</i> 11(6):1185-1189 (Apr. 2000). |

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|--------------------|---|---|----------------|
| C29 * | HORI, R., et al., "Gene transfection of H25A mutant heme oxygenase-1 protects cells against hyperoxide-induced cytotoxicity," <i>J. Biol. Chem.</i> 277(12):10712-10718 (Mar. 2002). | | |
| C30 * | ISHIKAWA, K., et al., "Expression of rat heme oxygenase in <i>Escherichia coli</i> as a catalytically active, full length form that binds to bacterial membranes," <i>Eur. J. Biochem.</i> 202:161-165 (1991). | | |
| C31 * | IYER, S., et al., "Characterization and biological significance of immunosuppressive peptide D2702.75-84 (E → V) binding protein," <i>J. Biol. Chem.</i> 273(5):2692-2697 (1998). | | |
| C32 * | JUAN, S-H., et al., Adenovirus-mediated heme oxygenase-1 gene transfer inhibits the development of atherosclerosis in apolipoprotein E-deficient mice," <i>Circulation</i> 104:1519-1525 (2001). | | |
| C33 * | KATORI, M., et al., "Heme oxygenase-1 overexpression exerts cytoprotective effects against ischemia/reperfusion injury via anti-apoptotic pathway," No. 843, <i>Conf. Proc. Transplant 2001</i> , The Joint American Transplant Meeting, Chicago, IL (May 11 - 16, 2001). | | |
| C34 * | KE, B., et al., "Heme oxygenase-1 gene transfer prevents Fas/Fas ligand-induced apoptosis <i>in vitro</i> and improves allograft function <i>in vivo</i> ," No. 2, <i>Conf. Proc. Transplant 2001</i> , The Joint American Transplant Meeting, Chicago, IL (May 11 - 16, 2001). | | |
| C35 * | KUEMMERLE, N.B., et al., "Gene expression after intrarenal injection of plasmid DNA in the rat," <i>Pediatr. Nephrol.</i> 14(2):152-157 (2000). | | |
| C36 * | LEDLEY, F.D., "Pharmaceutical approach to somatic gene therapy," <i>Pharm. Rev.</i> 13(11):1595-1614 (Nov. 1996). | | |
| C37 * | LEE, P.J., et al., "Overexpression of heme oxygenase-1 in human pulmonary epithelial cells results in cell growth arrest and increased resistance to hyperoxia," <i>Proc. Natl. Acad. Sci. USA</i> 93(19):10393-10398 (Sep. 1996). | | |
| C38 * | LEE, R., et al., "Isolated lung liposome-mediated gene transfer produces organ-specific transgenic expression," <i>Ann. Thorac. Surg.</i> 66:903-907 (1998). | | |
| C39 * | LEVINE, F., et al., "Towards gene therapy of diabetes mellitus," <i>Mol. Med. Today</i> 5:165-171 (Apr. 1999). | | |
| C40 * | LI, X.K., "Prolonged survival of rat liver allografts transfected with Fas ligand-expressing plasmid," <i>Transplantation</i> 66:1416-1423 (1998). | | |
| C41 | MAGEE, J.C., et al., "Gene transfer of immunosuppressive peptides B2702 and RDP1257 prolongs allograft survival: evidence suggesting a role for heme oxygenase-I," <i>Transplant. Proc.</i> 31(1-2):1194-1194 (Feb. - Mar. 1999). | | |
| C42 | MAINES, M., "Zinc protoporphyrin is a selective inhibitor of heme oxygenase activity in the neonatal rat," <i>Biochim. Biophys. Acta</i> 673:339-350 (1981). | | |
| C43 * | MARCONI, P., et al., "Replication-defective herpes simplex virus vectors for gene therapy <i>in vivo</i> ," <i>Proc. Natl. Acad. Sci. USA</i> 93(21):11319-11320 (Oct. 1996). | | |
| C44 | MARTASEK, P., et al., "Properties of human kidney heme oxygenase: inhibition by synthetic heme analogues and metalloporphyrins," <i>Biochem. Biophys. Res. Commun.</i> 157(2):480-487 (Dec. 1988). | | |
| C45 * | McCLAIN, S., et al., "Functional consequences of adenovirus-mediated murine pancreatic gene transfer," <i>Human Gene Ther.</i> 8(6):739-746 (Apr. 1997). | | |
| C46 * | MELO, L.G., et al., "Gene therapy strategy for long-term myocardial protection using adeno-associated virus mediated delivery of heme oxygenase gene," <i>Circulation</i> 105:602-607 (2002). | | |
| C47 * | MILLER, N., et al., "Targeted vectors for gene therapy," <i>FASEB J.</i> 9(2):190-199 (Feb. 1995). | | |

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|--------------------|-----------------------|---|--|--|----------------|
| | C48 * | MOFFATT, S.D., et al., "Comparison between tacrolimus and cyclosporine as immunosuppressive agents compatible with tolerance induction by CD4/CD8 blockade," <i>Transplantation</i> 69(8):1724-1726 (Apr. 2000). | | | |
| | C49 * | MURUVE, D., et al., "Ex vivo adenovirus-mediated gene therapy leads to long-term expression in pancreatic islet transplants," <i>Transplantation</i> 64(3):542-546 (1997). | | | |
| | C50 * | NAKAMURA, N., et al., "Early biological effect of <i>in vivo</i> gene transfer of platelet-derived growth factor (PDGF)-B into healing patellar ligament," <i>Gene Ther.</i> 5(9):1165-1117 (Sep. 1998). | | | |
| | C51 | NEIL, T.K., et al., "Modulation of corneal heme oxygenase expression by oxidative stress agents," <i>J. Ocular Pharmacol. Therap.</i> 11(3):455-468 (1995). | | | |
| | C52 * | NOVOGRODSKY, A., et al., "Immune stimulatory properties of metalloporphyrins," <i>J. Immunol.</i> 143(12):3981-3987 (Dec. 1989). | | | |
| | C53 * | OMATA, Y., et al., "Crystallization and preliminary X-ray diffraction studies on the water soluble form of rat heme oxygenase-1 in complex with heme," <i>Acta Cryst. D54</i> :1017-1019 (1998). | | | |
| | C54 * | ORKIN, S., et al., <i>Report and Recommendations of the Panel to Assess the NIH Investment in Research on Gene Therapy</i> , National Institutes of Health: Bethesda, MD (Dec. 1995). | | | |
| | C55 * | OTTERBEIN, L., et al., "Carbon monoxide has anti-inflammatory effects involving the mitogen-activated protein kinase pathway," <i>Nat. Med.</i> 6(4):422-428 (Apr. 2000). | | | |
| | C56 | PILEGGI, A., et al., "Absence of inducible nitric oxide synthase, and heme oxygenase01 upregulation result in improved islet graft function," No. 833, <i>Conf. Proc. Transplant 2001</i> , The Joint American Transplant Meeting, Chicago, IL (May 11 - 16, 2001). | | | |
| | C57 * | QIN, L., et al., "Multiple vectors effectively achieve gene transfer in a murine cardiac transplant model," <i>Transplantation</i> 59:809-816 (1995). | | | |
| | C58 * | QIN, L., et al., "Retrovirus-mediated transfer of viral IL-10 gene prolongs murine cardiac allograft survival," <i>J. Immunol.</i> 156:2316-2323 (1996). | | | |
| | C59 | RADAELLI, C., "Induction of heme oxygenase-1 improves rat liver transplantation survival by inhibiting apoptosis," No. 410, <i>Conf. Proc. Transplant 2001</i> , The Joint American Transplant Meeting, Chicago, IL (May 11 - 16, 2001). | | | |
| | C60 * | RAJU, V., et al., "Coordinated expression and mechanism of induction of HSP32 (heme oxygenase-1) mRNA by hyperthermia in rat organs," <i>Biochim. Biophys. Acta</i> 1217:273-280 (1994). | | | |
| | C61 | RIBEIRO, M., et al., "Inhibition of apoptosis in pancreatic β cells and islets by direct transfer of heme oxygenase-1 protein fused to a protein transduction domain (PTD)," No. 1025, <i>Conf. Proc. Transplant 2001</i> , The Joint American Transplant Meeting, Chicago, IL (May 11 - 16, 2001). | | | |
| | C62 * | ROTENBERG, M.O., et al., "Characterization of a cDNA-encoding rabbit brain heme oxygenase-2 and identification of a conserved domain among mammalian heme oxygenase isozymes: possible heme-binding site," <i>Arch. Biochem. Biophys.</i> 290(2):336-344 (Nov. 1991). | | | |
| | C63 | ROZA, A., et al., "AMD6221, a novel nitric oxide scavenger, decreases heme protein nitrosylation and prolongs cardiac allograft survival," No. 365, <i>Conf. Proc. Transplant 2001</i> , The Joint American Transplant Meeting, Chicago, IL (May 11 - 16, 2001). | | | |
| | C64 * | RUDINGER, J., "Characteristics of the amino acids as components of a peptide hormone sequence," <i>Peptide Hormones</i> , pp. 1-7, J.A. Parsons (ed.), University Park Press: Baltimore, MD (1976). | | | |
| | C65 * | SCHMITT, M.P., "Utilization of host iron sources by <i>Corynebacterium diphtheriae</i> : identification of a gene whose product is homologous to eukaryotic heme oxygenases and is required for acquisition of iron from heme and hemoglobin," <i>J. Bact.</i> 179(5):838-845 (1997). | | | |

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| Sheet | 5 | of | 6 | Application Number | 10/782,260 |
| | | | | Filing Date | February 18, 2004 |
| | | | | First Named Inventor | BUELOW, Roland |
| | | | | Art Unit | To be assigned |
| | | | | Examiner Name | To be assigned |
| | | | | Attorney Docket Number 33861/US/TAL/NHT ([A-63708-6] 465840-524) | |

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|--------------------|-----------------------|---|----------------|
| | C66 * | SCHULER, W., et al., "SDZ RAD, a new rapamycin derivative: pharmacological properties <i>in vitro</i> and <i>in vivo</i> ," <i>Transplantation</i> 64(1):32-35 (Jul. 1997). | |
| | C67 * | SCHULLER, D.J., "Crystal structure of heme oxygenase-1," <i>Nat. Struct. Biol.</i> 6(9):860-867 (Sep. 1999). | |
| | C68 * | SHAKED, A., et al., "Retroviral-mediated gene transfer into rat experimental liver transplant," <i>Transplantation</i> 57:32-34 (1994). | |
| | C69 * | SINAL, C.J., et al., "Liver transplantation induces cytochrome P450 1A1 dependent monooxygenase activity in rat lung and kidney," <i>Can. J. Physiol. Pharmacol.</i> 73:146-152 (1995). | |
| | C70 * | SOARES, M.P., et al., "Expression of heme oxygenase-1 can determine cardiac xenograft survival," <i>Nat. Med.</i> 4(9):1073-1077 (Sep. 1998). | |
| | C71 * | SONG, Y.K., et al.; "Enhanced gene expression in mouse lung by prolonging the retention time of intravenously injected plasmid DNA," <i>Gene Ther.</i> 5(11):1531-1537 (1998). | |
| | C72 | SQUIERS, E., et al., "Prolongation of porcine islet xenograft survival in mice after therapy with immunosuppressive peptides," <i>Transplantation</i> 66(11):1558-1565 (Dec. 1998). | |
| | C73 * | TEMPLETON, N., et al., "New Direction in Liposome Gene Delivery," <i>Mol. Biotechnol.</i> 11(2):175-180 (Apr. 1999). | |
| | C74 * | TENHUNEN, R., et al., "Microsomal Heme Oxygenase," <i>J. Biol. Chem.</i> 244(23):6388-6394 (Dec. 1969). | |
| | C75 * | VERMA, I., et al., "Gene therapy – promises, problems and prospects," <i>Nature</i> 389(6648):239-242 (Sep. 1997). | |
| | C76 * | VORBURGER, S., et al., "Adenoviral Gene Therapy," <i>Oncologist</i> 7(1):46-59 (Feb. 2002). | |
| | C77 * | WANG, J., et al., "Adenovirus-mediated gene transfer into rat cardiac allografts," <i>Transplantation</i> 61(12):1726-1729 (Jun. 1996). | |
| | C78 | WANG, N., et al., "Xenograft accommodation: expression of heme oxygenase-1 protects endothelial cells from xenoserum-mediated apoptosis," No. 993, <i>Conf. Proc. Transplant 2001</i> , The Joint American Transplant Meeting, Chicago, IL (May 11 – 16, 2001). | |
| | C79 * | WEISS, G., et al., "Comparative effects of heme and metalloporphyrins on interferon- γ -mediated pathways in monocytic cells (THP-1)," <i>Proc. Soc. Exp. Biol. Med.</i> 202(4):470-475 (Apr. 1993). | |
| | C80 * | WILKS, A., et al., "Rat liver heme oxygenase: high level expression of a truncated soluble form and nature of the meso-hydroxylating species," <i>J. Biol. Chem.</i> 268(30):22357-22362 (Oct. 1993). | |
| | C81 * | WILLIS, D., et al., "Heme oxygenase: a novel target for the modulation of the inflammatory response," <i>Nat. Med.</i> 2(1):87-90 (Jan. 1996). | |
| | C82 * | WOO, J., et al., "Alleviation of graft-versus-host disease after conditioning with cobalt-protoporphyrin, an inducer of heme oxygenase-1," <i>Transplantation</i> 69(4):623-633 (Feb. 2000). | |
| | C83 * | WRINGER, E.J., et al., "Antagonizing leukotriene B4 receptors delays cardiac allograft rejection in mice," <i>Transplantation</i> 67(6):808-815 (Mar. 1999). | |
| | C84 * | XIA, Q.I., et al., "Production of high titer recombinant adeno-associated virus vectors in the absence of helper adenovirus," <i>J. Virol.</i> 72(3):2224-2232 (Mar. 1998). | |
| | C85 * | YOSHIDA, T., et al., "Human heme oxygenase cDNA and induction of its mRNA by hemin," <i>Eur. J. Biochem.</i> 171(3):457-461 (Feb. 1988). | |

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|--------------------|-----------------------|---|----------------|
| | C86 | ZHU, N., et al., "Systemic gene expression after intravenous DNA delivery into adult mice," <i>Science</i> 261(5118):208-211 (Jul. 1993). | |

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